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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/748,897	12/29/2003	Anthony Joonkyoo Yun	PALO-002	7432

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EXAMINER	
RAMACHANDRAN, UMAMAHESWARI	
ART UNIT	**PAPER NUMBER**
1617	

MAIL DATE	DELIVERY MODE
11/29/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/748,897	YUN ET AL.	
	Examiner	Art Unit	
	Umamaheswari Ramachandran	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 September 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1, 3, 4, 11 – 63 is/are pending in the application.

4a) Of the above claim(s) 29-40, 41-61 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) 1, 3-4, 11-28, 41, 62, 63 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The examiner notes the receipt of the filing of Terminal Disclaimer, amendments and remarks received in the office on 9/11/2007 amending claims 1, 3, 4, 20 and adding new claims 62 and 63. Claims 2, 5-10 have been canceled and claims 29-61 are withdrawn from consideration. Claims 1, 3, 4, 11-28, 41, 62, 63 are pending.

Response to Remarks

The rejection of claims 1-7, 9, 10, 14, 16, 19-22, 28, 41 under 35 U.S.C. 102(b) as being anticipated by Gambardella et al. (Metabolism, 46, 3, March, 1999, p 291-297), the rejection of claims 1, 3, 4, 21, 28, 41 anticipated by Brevetti et al. (Brief communications, Nov 1981, p 938-941), the rejection of claims 1, 21, 41 anticipated by Nordling et al. (E Urol, 1992, 21, 328-331), the rejection of claims 1, 3, 4, 11-12, 15, 17, 21, 22, the rejection of claims 1, 3, 4, 11-12, 15, 17, 21, 22 anticipated by Majcherczyk et al. (Br J Pharmacol, 1987, 91(4), 711-4), the rejection of claims 1, 21, 23-25, 28 anticipated by Davies et al. (The J of Intl Med Research, 1988, 16, 173-181), the rejection of claims 1, 26-27 anticipated by Hill et al. (U.S. 6,449,507) are withdrawn due to the amendment of claim 1. Applicants' amendment necessitated the modified rejections presented in this office action. The office action is made Final.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3, 4, 13, 14, 16, 18-22, 28, 41, 62, 63 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gambardella et al. (Metabolism, 46, 3, March, 1999, p 291-297).

Gambardella et al. teach a method of treating a condition due to deficient parasympathetic activity associated with elevated basal metabolic rate in cancer patients by oral administration of propranolol (see Abstract, p 295, para 1, lines 1-8, p 296, para 4, 1-5). The reference teaches the autonomic nervous system dysfunction in cancer patients with elevated basal metabolic rate, there is an unbalanced sympathetic (SNS)/parasympathetic nervous system (PNS) ratio which may exist due to SNS overactivity in cancer patients due to impaired PNS activity. The reference further teaches that beta-blocker such as propranolol administration (for 6 days, twice daily, see experimental design) may be useful to counteract the negative impact of the SNS on metabolic pathways (p 297, para 3 continued on 298). The reference teaches the sympathetic bias in at least a portion of autonomic nervous system, abnormality characterized by sympathetic bias, parasympathetic bias with an unbalanced SNS/PNS ratio with high SNS activity and low PNS activity. Due to the modulation in the sympathetic and parasympathetic activities in the autonomic nervous system a stage is reached where sympathetic and parasympathetic activities are substantially equal during the treatment of cancer by oral administration of propranolol and also by balancing the autonomic nervous system dysfunction in cancer patients by administration of propranolol the parasympathetic activity is increased.

It would have been obvious to one of ordinary skill in the art at the time of the invention that oral administration of propranolol modulates or balances the sympathetic and parasympathetic activities of the autonomic nervous system in cancer patients and when balancing such activities a stage is reached where sympathetic and parasympathetic activities are substantially equal.

The reference does not explicitly teach a method of treating conditions caused by abnormality in autonomic nervous system wherein the abnormality is characterized by normal sympathetic activity.

It would have been obvious to one of ordinary skill in the art at the time of the invention to administer a beta blocker such as propranolol in treating a condition caused by abnormality in autonomic nervous system where the abnormality is characterized by normal sympathetic activity. The motivation to do so is provided by Gambardella et al. because the reference teaches that propranolol is effective in the treatment of abnormality in autonomic nervous system. One of ordinary skill in the art would have been motivated to treat abnormality in autonomic nervous system characterized by normal sympathetic activity by administration of a beta blocker to modulate the sympathetic and parasympathetic activities because of expectation of success and to achieve the therapeutic effects in treating the disorder associated with the abnormality of autonomic nervous system.

Claims 1, 3, 4, 21, 28, 41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brevetti et al. (Brief communications, Nov 1981, p 938-941).

Brevetti et al. teach an intravenous and oral administration of propranolol for the treatment of Shy-Drager syndrome, a severe degeneration of the autonomic nervous system. The reference further teaches that orthostatic hypotension a condition of Shy-Drager syndrome is mainly dependent on peripheral vasodilation without the normal response of postural vasoconstriction and may be a consequence of an imbalance of alpha and beta adrenoreceptor activity in peripheral nervous system and that beta-blockade may provide an effective means of treating orthostatic hypotension in patients with Shy-Drager syndrome (p 940 para 2, lines 1-5, continued on page 941). The reference teaches a sympathetic bias and a parasympathetic bias in at least a portion of said autonomic nervous system.

It would have been obvious to one of ordinary skill in the art at the time of the invention that administration of propranolol modulates or balances the sympathetic and parasympathetic activities of the autonomic nervous system by treating Shy-Drager syndrome condition and when balancing such activities a stage is reached where sympathetic and parasympathetic activities are substantially equal.

Claims 1, 21, are rejected under 35 U.S.C. 103(a) as being unpatentable over Nordling et al. (E Urol, 1992, 21, 328-331).

Nordling et al. teach the administration of non-selective beta-adrenergic receptor antagonist propranolol reduced the urethral inflammation (see Abstract). The reference also teaches that severity of urethral inflammation was increased in spontaneous hypertensive rats, which have an increased sympathetic tone as compared to the

normotensive rats (see Abstract). Hence by reducing urethral inflammation by administration of propranolol, sympathetic tone is decreased.

It would have been obvious to one of ordinary skill in the art at the time of the invention that administration of propranolol modulates or alters the sympathetic and parasympathetic activities of the autonomic nervous system by treating urethral inflammation and when balancing such activities a stage is reached where sympathetic and parasympathetic activities are substantially equal.

Claims 1, 3, 4, 11-12, 15, 17, 21, 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Majcherczyk et al. (Br J Pharmacol, 1987, 91(4), 711-4).

Majcherczyk et al. teaches the increase in renal sympathetic nerve activity by propranolol in hypertensive rats (Abstract). Hypertension is an age-associated condition and the reference inherently teaches the sympathetic and non-sympathetic bias and a low sympathetic activity.

It would have been obvious to one of ordinary skill in the art at the time of the invention that administration of propranolol modulates or alters the sympathetic and parasympathetic activities of the autonomic nervous system in the treatment of hypertension and when balancing such activities a stage is reached where sympathetic and parasympathetic activities are substantially equal.

Claims 1, 21, 23-25, 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Davies et al. (The J of Intl Med Research, 1988, 16, 173-181).

Davies et al. teach the administration of ibuprofen, a non-steroidal anti-inflammatory drug along with an anti-hypertensive agent and a beta-blocker such as propranolol (see Abstract) to group of patients with hypertension.

It would have been obvious to one of ordinary skill in the art at the time of the invention that administration of propranolol modulates or alters the sympathetic and parasympathetic activities of the autonomic nervous system in the treatment of hypertension and when balancing such activities a stage is reached where sympathetic and parasympathetic activities are substantially equal and the reference teach that parasympathetic nerves influence cerebral blood flow during hypertension.

Claims 1, 26-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hill et al. (U.S. 6,449,507).

Hill et al. teach the stimulation of nerve or nerve fibers (vagus nerve fibers, hypoglossal nerve fibers, phrenic nerve fibers, parasympathetic nerve fibers, and sympathetic nerve fibers, a vagal nerve) by using electrodes and electrical current and further comprising beta-blockers such as propranolol in a medical procedure such as beating heart surgery, arrythmias, vascular surgery, neurosurgery etc which are aging associated conditions (col. 2, lines 61-65, col. 17, claim 1, claim 10, col. 18, claim 19, co. 20, claim 50).

It would have been obvious to one of ordinary skill in the art at the time of the invention that administration of propranolol modulates or alters the sympathetic and parasympathetic activities of the autonomic nervous system as Hill teaches the

stimulation of parasympathetic and sympathetic nerve fibers and when balancing such activities a stage is reached where sympathetic and parasympathetic activities are substantially equal.

Response to Arguments

Applicants argue that Gambardella et al. fail or suggest teaching the element of treating a condition wherein modulating the autonomic nervous system results in substantially equal parasympathetic or sympathetic functions in at least a portion of the autonomic nervous system. In response, Gambardella et al. does not explicitly teach that modulating the autonomic nervous system results in substantially equal parasympathetic or sympathetic functions in at least a portion of the autonomic nervous system. However, the reference teach a method of treating a condition due to deficient parasympathetic activity associated with elevated basal metabolic rate in cancer patients by oral administration of propranolol and further teach that there is an unbalanced sympathetic (SNS)/parasympathetic nervous system (PNS) ratio which may exist due to SNS overactivity in cancer patients due to impaired PNS activity. Hence by treating or balancing the autonomic nervous system by administration of propranolol the sympathetic activity is decreased and parasympathetic activity is increased and a stage is reached where parasympathetic or sympathetic functions are substantially equal. Hence it would have been obvious to one of ordinary skill in the art at the time of the invention that oral administration of propranolol modulates or balances the sympathetic and parasympathetic activities of the autonomic nervous system in cancer patients

because when balancing such activities a stage is reached where sympathetic and parasympathetic activities are substantially equal.

Conclusion

No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Umamaheswari Ramachandran whose telephone number is 571-272-9926. The examiner can normally be reached on M-F 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER